



## RECENT PROGRESS IN PHYSIOLOGY.<sup>1</sup>

BY HENRY P. BOWDITCH, M. D.

### VASO-MOTOR MECHANISM.

IN the report on the progress of physiology published in this journal in January, 1875, an account was given of the experiments which led Goltz to the conclusion that vascular dilatation in any part of the body, following section of the nerve supplying that part, is due to irritation of vaso-dilator nerve fibres, and not, as generally believed, to paralysis of vaso-constrictor fibres. Allusion was made also to the observations of Putzeys and Tarchanoff, pupils of Goltz, who found, in opposition to their teacher, that electrical irritation of the peripheric end of a divided sciatic nerve causes always a contraction of the vessels of the limb, which gives place only after several minutes to a dilatation attributable to exhaustion. In this report an attempt will be made to present briefly the principal results reached by various observers who have recently endeavored to contribute to our knowledge of the vaso-motor mechanism.

In the first place it should be mentioned that Vulpian, in his *Leçons sur l'appareil vaso-moteur*,<sup>2</sup> which appeared shortly after Goltz's paper, criticised the statements therein contained, and asserted most emphatically that in numerous experiments on curarized and chloralized dogs, he had always found a contraction and never a dilatation of the vessels of the foot to follow an electrical irritation of the peripheric end of the divided sciatic nerve. Equally decided results were obtained by Eulenburg and Landois<sup>3</sup> in their experiments on rabbits and dogs, the effect of irritation of the sympathetic and sciatic nerves being always a vascular contraction as indicated by a fall of temperature in the part.

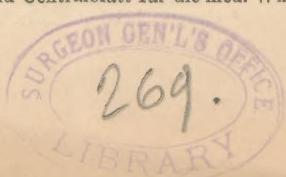
Goltz, however, in a second article,<sup>4</sup> reasserted and defended his former opinions, maintaining that if, in accordance with current views on the subject, the vaso-constrictor nerves are supposed to be in a state of life-long tonic activity, it is unreasonable to attribute to their exhaustion the vascular dilatation which, after a short primary constriction, results from the irritation of a divided sciatic nerve, especially as the primary constriction is never so great as that which is constantly main-

<sup>1</sup> Reprinted from the Boston Medical and Surgical Journal, July 19 and 26, 1877.

<sup>2</sup> Vol. ii., page 480.

<sup>3</sup> Virchow's Archiv, lxvi. and lxviii., and Centralblatt für die med. Wiss., 1877, page 104.

<sup>4</sup> Pflüger's Archiv, xi. 52.



tained during life. He brought forward, moreover, the following experiment, to support his theory: The spinal cord of a strong young dog was divided at the level of the last rib. A few days later, after the temperature of the hind limbs (which rises as the result of the operation) had returned to its normal level, both sciatic nerves were divided as high as possible in the thigh. After another interval of a few days, to allow the temperature to subside, the peripheric end of one of the sciatic nerves was cut away in successive small pieces from above downward, or nicked with scissors through its whole length, or hammered with Heidenhain's so-called "tetano-motor," or treated with strong sulphuric acid. The result of any one of these methods of irritation was to cause an immediate rise in the temperature of the leg operated on, the difference between the two legs amounting frequently to 10° C.

The question then arose, Why does irritation of the sciatic nerve under these particular circumstances cause dilatation of the vessels of the foot, while under ordinary circumstances the opposite result is produced? The first experiments throwing light on this question were those of Ostroumoff.<sup>1</sup> This observer, operating on curarized dogs, found that, while tetanic stimulation of the peripheric end of a *freshly divided* sciatic nerve caused a prolonged contraction of the vessels of the foot, indicated by a decided fall of temperature, the same stimulation applied to a nerve *three or four days after section* was followed by a rapid rise of temperature.

He found also that stimulation by single induction shocks, applied at intervals of five seconds, caused, even when the nerves were freshly divided, a rise of temperature in the foot. The same result could also be produced, though with difficulty, by certain very weak tetanic irritations. To explain these results Ostroumoff assumed the existence in the sciatic nerve of two sorts of vaso-motor fibres, namely: (1) vaso-constrictors, irritable by tetanic stimulation, and rapidly degenerating after section; (2) vaso-dilators, irritable by slow rhythmical stimulation, and degenerating slowly after section.

Kendall and Luchsinger,<sup>2</sup> at about the same time, but entirely independent of Ostroumoff, reached almost identical results in a series of experiments on dogs, cats, rabbits, and ducks. The rhythmical stimulation employed by these observers was rather more rapid (intervals of 0.5" to 2") than that used by Ostroumoff, which perhaps accounted for the greater difficulty which they had in causing vascular dilatation by irritating a freshly divided nerve.

Masius and Vaulair<sup>3</sup> were led by their experiments to conclusions very similar to those of Goltz, since they found that either electrical or

<sup>1</sup> Pflüger's Archiv, xii. 219.

<sup>2</sup> Pflüger's Archiv, xiii. 197.

<sup>3</sup> Gazette hebdomadaire, October 8, 1875.

mechanical stimulation of the sciatic nerve caused in almost every case (and nearly always immediately) a dilatation of the vessels of the foot. Their conception of the mechanism of vaso-motor action will be given in the latter part of this report.

Lépine,<sup>1</sup> in a series of well-devised experiments on curarized dogs, discovered, as did the above-mentioned German observers, that the time elapsing between the section and the irritation of the nerve affected the result of the irritation, the same stimulation causing in freshly cut nerves a contraction, and in nerves cut several days previously a dilatation of the cutaneous blood-vessels. He did not, however, like Ostroumoff and others, attribute this difference to a slower degeneration of vaso-dilator nerve fibres, for he found that stimulation of a recently divided nerve, which while the temperature of the foot was 30° C. had no marked effect on the size of the blood-vessels, produced a distinct dilatation (that is, a rise of temperature) when the foot had been previously cooled by immersion in water of 10° C., and an equally marked contraction (that is, a fall of temperature) when the foot had been warmed by plunging it into water of 60° C. He also found that if the rise of temperature in the foot, which naturally follows section of the sciatic nerve, was in any way prevented, as by a previous operation on the skull involving considerable haemorrhage, stimulation of the peripheral end of the nerve caused not a contraction but a dilatation of the cutaneous blood-vessels. Endeavoring to determine more accurately the mechanism of these vaso-motor phenomena, Lépine found that a preliminary immersion of the foot in warm water caused a stimulation of the nerve to constrict the cutaneous vessels, even though the temperature of the foot had from other reasons (for example, curarization) fallen below the point at which a previous stimulation had caused a vascular dilatation. Lépine therefore concludes that it is not so much the temperature of the part which influences the result of stimulation of the nerve as the condition of the terminal nervous apparatus which regulates the calibre of the blood-vessels. This terminal apparatus (perivascular ganglia) has, according to Lépine, purely constrictor functions, and keeps the vascular walls in a constant state of tonic contraction. When stimulated by cold to its highest activity, it so far reduces the size of the blood-vessels that irritation of the vaso-constrictor fibres of the sciatic can effect no further reduction, while the vaso-dilator fibres, also contained in the sciatic and affected therefore by the same stimulation, enlarge the vessels which cold has constricted.

On the other hand, when heat has lowered the tonic activity of the terminal apparatus, and caused dilatation of the vessels, the conditions presented are favorable for the action of the vaso-constrictor and unfavorable for that of the vaso-dilator fibres. The result of the experi-

<sup>1</sup> Société de Biologie, March 4, 1876.

ment above alluded to is explained by Lépine on the supposition that the tonicity of the terminal apparatus reduced to a minimum by immersion in warm water had not been restored at the time of the stimulation, though the curare had caused a lowering of the temperature of the whole body. Hence the cutaneous blood-vessels were constricted by stimulation of the sciatic nerve in a way usually observed only in connection with a high temperature of the part.

In this connection is to be noted an observation of Eckhard,<sup>1</sup> who found, in studying the blood-vessels of the rabbit's ear, that in the earlier stages of curarization, when the vessels were of normal size or dilated, stimulation of a sensitive nerve caused a reflex vascular contraction, while in the later stages, characterized by constriction of the vessels, the same stimulus caused a reflex dilatation.

Lépine's conception of the vaso-motor mechanism as consisting of a terminal apparatus and two sorts of nerve fibres is the same that has, with various modifications, been adopted by nearly all recent observers. Thus Huizinga,<sup>2</sup> as the result of his experiments on curarized frogs, concludes that the vaso-motor apparatus consists of

I. Local ganglia presiding over the rhythmical contraction of the vessels.

II. Spinal vaso-constrictor fibres going directly to the arteries.

III. Spinal nerve fibres inhibiting the local ganglia.

IV. Inhibitory fibres from the skin to the neighboring ganglia.

A local irritation of the skin may cause either vascular dilatation through IV. or vascular constriction through II. Which result is produced depends upon the locality and the intensity of the irritation. The nearer the irritated part to the blood-vessels under observation, and the stronger the stimulus, the greater is the tendency to the production of a vascular dilatation instead of a constriction.

Masius and Valnair<sup>3</sup> hold essentially the same views, except that they regard the spinal vaso-constrictor fibres (II.) as acting through the local ganglia instead of directly on the vessels, and they admit the existence of exciting as well as inhibitory fibres running from the skin to the neighboring ganglia.

All recent investigators unite in assuming the existence of nerve cells in or near the vascular walls to account for the recovery of their condition of tonic contraction after section of the spinal nerves, but it should be borne in mind that histologists have as yet only rarely succeeded in bringing anatomical evidence in support of this assumption.

Inasmuch, however, as we find in the walls of the small intestine a plexus of nerve cells and fibres which seems to preside over the move-

<sup>1</sup> Beiträge, vii. 83.

<sup>2</sup> Pflüger's Archiv, xi. 207.

<sup>3</sup> Loco citato.

ments of that organ, and to be subjected to both excitation and inhibition through nerve fibres connecting it with the cerebro-spinal centres, it is not improbable that the blood-vessels may be subjected to similar control.

Ostromoff's observations have shown that this peripheric vaso-motor apparatus, whatever may be its anatomical structure, is able to hold the blood-vessels in a state of tonic contraction after division of the spinal nerves. It was even found that when the blood tension was increased to double its normal amount by irritation of the splanchnic nerves of a dog, one of whose sciatic nerves had been divided, the temperature rose as little in the paralyzed as in the normal limb, showing that the activity of the vascular walls must be independent of influences coming from the cerebro-spinal centres. If, however, the experiment was many times repeated, it was found that finally stimulation of the splanchnic nerves caused a great dilatation of the vessels in the paralyzed foot, and but little or none in those of the normal limb. Hence it must be concluded that vessels which are still in connection with the central nervous system are better able to resist the dilating effect of increased blood tension because they are less easily fatigued.

The theory that the spinal nerves contain two anatomically distinct sorts of nerve fibres has been adopted by nearly all recent investigators to explain the fact that stimulation of these nerves may be followed either by vascular constriction or dilatation. Onimus<sup>1</sup> has, however, been led to the conclusion that inhibitory phenomena resulting from the stimulation of a nerve do not necessarily prove the existence of special inhibitory fibres in that nerve. He found, in the first place, that a single moderate irritation of the vagus, instead of arresting the heart, produced a contraction of that organ;<sup>2</sup> also that, when in a curarized animal the heart beats had been reduced to forty or fifty per minute, it was possible, by irritating the vagus or the heart itself with induction shocks at the rate of sixty per minute, to compel the heart to contract synchronously with the electrical stimulation. Analogous observations were made also on the intestines. Here it was found that ordinary tetanic stimulation arrested the peristaltic movements in the neighborhood of the part irritated, causing only a local contraction of the muscles directly between the electrodes, while a series of induction shocks following each other at about the rate of the normal peristaltic contractions (fifteen to eighteen per minute) increased the intensity of these movements.

Onimus therefore concludes that when electrical irritations are ap-

<sup>1</sup> Comptes rendus des Séances de l'Académie des Sciences. November 20, 1876. Tome Ixxxiii., page 988.

<sup>2</sup> It is possible, however, as shown by Donders (*Pflüger's Archiv*, i. 331), to produce an inhibitory effect upon the heart by irritating the vagus with a single induction shock.

plied to a nerve at a rate approaching that at which the impulses follow each other along the nerve in its normal condition, the stimulation produces a state of activity in the organs to which the nerve is distributed, but that when the rate of the irritations differs too widely from that of the normal impulses, a condition of inhibition is brought about. In accordance with this theory the production of vascular dilatation by slow rhythmical irritations of a spinal nerve, as observed by Ostromoff, depends upon an inhibition of vaso-constrictor fibres.

It will be observed that this theory affords no explanation of the fact that while tetanic stimulation of a freshly cut nerve causes vascular constriction, the same stimulation applied to a nerve several days after its division has the opposite effect. Moreover, the vaso-dilator fibres seem in many cases to run in channels anatomically distinct from those of the vaso-constrictor fibres. For instance, the chorda tympani seems to supply exclusively vaso-dilator and the cervical sympathetic vaso-constrictor fibres to the submaxillary gland and the tongue. To cases of this sort the theory of Onimus is hardly applicable. Even in the spinal nerves the courses of the two sorts of fibres seem, according to recent observations of Stricker,<sup>1</sup> to be to a certain extent distinct. The experiments were made on dogs whose spinal cords had been divided a few days before between the dorsal and lumbar regions, by the intervertebral method of Goltz. After the temperature in the hind limbs had fallen to its normal level, the cord was exposed in the lumbar region and the spinal roots subjected to division and stimulation. It was thus found that mechanical as well as electrical stimulation of the peripheric end of the divided *posterior* roots of the fourth and fifth lumbar nerves caused always an elevation of temperature in the foot of the corresponding side. The same stimulation applied to the anterior roots of the same nerves had no constant effects on the temperature of the foot. The author therefore concludes that some, at least, of the vaso-dilator fibres of the foot have a direct course through the posterior roots of the sciatic nerve. Other vaso-motor fibres were found to leave the cord by the upper lumbar and lower dorsal nerve roots. From the fact that two hours after destruction of the whole spinal cord below the fourth dorsal vertebra section of the sciatic nerve caused an elevation of the temperature of the foot, Stricker concludes that vaso-constrictor fibres leave the cord as high as the fourth dorsal nerve, the supposition that the vascular dilatation following section of the nerve might be produced by a mechanical irritation of the vaso-dilator fibres contained therein (according to Goltz's theory) being disproved by the fact that immediately after the section electrical irritation of the peripheric end of the divided nerve was followed by a distinct vascular constriction.

Stricker's experiments have been repeated and his work criticised by

<sup>1</sup> Wiener Sitzungsberichte, July 20, 1876.

Cossy,<sup>1</sup> who points out that, though irritation of the above-mentioned posterior roots may cause vascular dilatation, there is a great difference between the phenomena thus produced and those observed after the irritation of a well-recognized vaso-dilator nerve, such as the chorda tympani or the glosso-pharyngeal,—a difference not only in the constancy and degree, but also in the time of appearance and duration of the resulting dilatation. He therefore regards the existence of vaso-dilator fibres in the posterior roots of the lumbar nerves as not demonstrated.

*Collateral Innervation.*—When vascular tonicity is restored in a region which has been separated from its nerve centres, the explanation usually given of the phenomenon is that the terminal apparatus has assumed, in the absence of impulses coming from the central nervous system, a higher degree of activity than it formerly possessed. Stricker<sup>2</sup> has, however, shown that this is not the only method by which such a result may be reached. He concludes from his experiments: first, that each vascular region is supplied by many vaso-constrictor nerves, which leave the cord at different places; secondly, that after division of the cord between the lumbar and dorsal regions the restoration of vascular tonicity in the hind limbs is effected by the vaso-constrictors which leave the dorsal cord above the point of division. He considers it probable that these vaso-constrictors have their centres in the spinal cord (or in the brain), and that they are of themselves too weak to maintain the tonicity of the vessels which they supply, but that after division of the cord they gradually acquire greater power. Stricker proposes the term “collateral innervation” to express this process.

*Antagonism of Vaso-Constrictor and Vaso-Dilator Nerves.*—The effect of simultaneous irritation of the two sorts of vaso-motor fibres has been studied by von Frey<sup>3</sup> by a method similar to that employed by Baxt<sup>4</sup> in the investigation of the inhibitory and accelerator nerves of the heart. The nerves chosen for this purpose were the chorda tympani and the cervical sympathetic of the dog. The effect of the irritation was measured by the amount of blood flowing from the veins of the submaxillary gland, as determined by the automatic recording apparatus described by Gaskell.<sup>5</sup> As the result of his experiments, von Frey concludes that when both nerves are subjected to maximum irritations the blood flows through the gland in the same way as if the sympathetic alone were irritated, and this is the case whether the two nerves are simultaneously or successively irritated. The influence of the chorda tympani, thus held in abeyance, reappears, however, in its full strength on the cessation of the irritation of its antagonist. It may,

<sup>1</sup> Archives de Physiologie, 1876, page 832.

<sup>2</sup> Wiener Sitzungsberichte, February 1, 1877.

<sup>3</sup> Ludwig's Arbeiten, 1876, page 89.

<sup>4</sup> Ludwig's Arbeiten, 1875, page 179.

<sup>5</sup> Ludwig's Arbeiten, 1876, page 45

therefore, be said that the activity of the chorda tympani produces a certain change in the vascular walls, in consequence of which the flow of blood becomes more rapid, and that the cervical sympathetic, while it cannot hinder this change from running its natural course, can (as long as it is itself active) prevent it from influencing the circulation.